11. Fmoc-Tyr(^{t}Bu)

to provide 10 mg of N-Ac-Tyr-Thr-Thr-Asn-Pro-Arg-Lys-Leu-Tyr-Asp-Tyr-NH_2.

EXAMPLE 6

N-Ac-Pro-Arg-Lys-Leu-Tyr-Asp-Tyr-NH_2

The title compound was prepared using the synthetic sequence described in Example 1 and using Fmoc-Tyr(^{t}Bu) as amino acid No. 1. The following amino acids were added using the conditions indicated:

No.	Amino Acid
2.	Fmoc-Asp(β-O^{t}Bu)
3.	Fmoc-Tyr(^{t}Bu)
4.	Fmoc-Leu
5.	Fmoc-Lys(Boc)
6.	Fmoc-Arg(Pmc)
7.	Fmoc-Pro

to provide N-Ac-Pro-Arg-Lys-Leu-Tyr-Asp-Tyr-NH_2 (4 mg). MS (FAB) m/z 995 $(M+H)^+$.

EXAMPLE 7

N-Ac-Pro-Arg-Lys-Leu-Tyr-Asp-NH_2

The title compound was prepared using the synthetic sequence described in Example 1. The following amino acids were added using the conditions indicated:

No.	Amino Acid
2.	Fmoc-Tyr(^{t}Bu)
3.	Fmoc-Leu
4.	Fmoc-Lys(Boc)
5.	Fmoc-Arg(Pmc)
6.	Fmoc-Leu

to provide N-Ac-Pro-Arg-Lys-Leu-Tyr-Asp-NH_2 (6 mg). MS (ESI) m/z 832 $(M+H)^+$.

EXAMPLE 8

line 18 → N-Ac-Pro-Glu-Lys-Arg-Tyr-Asp-Tyr-NH_2 (SEQ ID NO:39)

The title compound was prepared using the synthetic sequence described in Example 1 and using Fmoc-Tyr(^{t}Bu) as amino acid No. 1. The following amino acids were added using the conditions indicated:

No.	Amino Acid
2.	Fmoc-Asp(β-O^{t}Bu)

Please REPLACE the paragraph at page 4, line 29 with the following amended paragraph:

[FIG. 3]Figures 3(a) and 3(b) show[s] the DNA sequence (SEQ ID NO:12) of human plasminogen.

Please REPLACE the paragraph at page 8, line 18 with the following replacement paragraph:

A-Pro-Glu-Lys-Arg-Tyr-Asp-Tyr-Y (SEQ ID NO:39)

Please REPLACE the paragraph on page 46, line 12 with the following amended paragraph:

N-Ac-Pro-Arg-Lys-Leu-3-I-Tyr-Asp-Tyr-NH_2 (SEQ ID NO:[13]6)

Please REPLACE the paragraph on page 47, line 1 with the following amended paragraph:

N-Ac-Pro-Arg-Lys-Leu-Tyr-Asp-3-I-Tyr-NH_2 (SEQ ID NO:[14]18)

Please REPLACE the paragraph on page 47, lines 17-19 with the following amended paragraph:

Preparation and separation of a mixture N-Ac-Pro-Arg-Lys-Leu-Tyr-Asp-3-I^{125}-Tyr^{535}-NH_2 and N-Ac-Pro-Arg-Lys-Leu-3-I^{125}-Tyr^{533}-Asp-Tyr-NH_2 (SEQ ID NO:[13]6) and (SEQ ID NO:[14]18) respectively.

Please REPLACE the paragraph on page 50, lines 4-12 with the following amended paragraph:

The effect of kringle 5 peptide fragments on endothelial cell proliferation was determined *in vitro* using the above described endothelial cell proliferation assay. For these experiments, kringle 5 peptide fragments [was]were prepared as illustrated in Examples 1 through 14 and tested at various concentrations ranging from about 100 to 1000 pM with bFGF used as a maximum proliferation control. The kringle 5 peptide

EXAMPLE 7

N-Ac-Pro-Arg-Lys-Leu-Tyr-Asp-NH_2

The title compound was prepared using the synthetic sequence described in Example 1. The following amino acids were added using the conditions indicated:

No. Amino Acid
2. Fmoc-Tyr('Bu)
3. Fmoc-Leu
4. Fmoc-Lys(Boc)
5. Fmoc-Arg(Pmc)
6. Fmoc-Leu

to provide N-Ac-Pro-Arg-Lys-Leu-Tyr-Asp-NH_2 (6 mg). MS (ESI) m/z 832 $(M+H)^+$.

EXAMPLE 8

N-Ac-Pro-Glu-Lys-Arg-Tyr-Asp-Tyr-NH_2 (SEQ ID NO:39)

The title compound was prepared using the synthetic sequence described in Example 1 and using Fmoc-Tyr('Bu) as amino acid No. 1. The following amino acids were added using the conditions indicated:

No. Amino Acid
2. Fmoc-Asp(β-O'Bu)
3. Fmoc-Tyr('Bu)
4. Fmoc-Arg(Pmc)
5. Fmoc-Lys(Boc)
6. Fmoc-Glu
7. Fmoc-Pro

to provide N-Ac-Pro-Glu-Lys-Arg-Tyr-Asp-Tyr-NH_2 (6 mg). MS (FAB) m/z (1101) $(M+H)^+$.

EXAMPLE 9

N-Ac-Arg-Lys-Leu-Tyr-Asp-Tyr-NH_2

The title compound was prepared using the synthetic sequence described in Example 1 and using Fmoc-Tyr('Bu) as amino acid No. 1. The following amino acids were added using the conditions indicated:

No. Amino Acid
2. Fmoc-Asp(β-O'Bu)
3. Fmoc-Tyr('Bu)
4. Fmoc-Leu
5. Fmoc-Lys(Boc)
6. Fmoc-Arg(Pmc)

to provide N-Ac-Arg-Lys-Leu-Tyr-Asp-Tyr-NH_2 (8 mg). MS (ESI) m/z 898 $(M+H)^+$.

EXAMPLE 10

N-Ac-Pro-Arg-Lys-Leu-3-I-Tyr-Asp-Tyr-NH_2 (SEQ ID NO: 6)

The title compound was prepared using the synthetic sequence described in Example 1 and using Fmoc-Tyr('Bu) as amino acid No. 1. The following amino acids were added using the conditions indicated:

No. Amino Acid
2. Fmoc-Asp(β-O'Bu)
3. Fmoc-3-I-Tyr('Bu)
4. Fmoc-Leu
5. Fmoc-Lys(Boc)
6. Fmoc-Arg(Pmc)
7. Fmoc-Pro

to provide N-Ac-Pro-Arg-Lys-Leu-3-I-Tyr-Asp-Tyr-NH_2 (2 mg). MS (ESI) m/z (1121) $(M+H)^+$.

EXAMPLE 11

N-Ac-Pro-Arg-Lys-Leu-Tyr-Asp-3-I-Tyr-NH_2 (SEQ ID NO: 18)

The title compound was prepared using the synthetic sequence described in Example 1 and using Fmoc-3-I-Tyr ('Bu) as amino acid No. 1. The following amino acids were added using the conditions indicated:

No. Amino Acid
2. Fmoc-Asp(β-O'Bu)
3. Fmoc-Tyr('Bu)
4. Fmoc-Leu
5. Fmoc-Lys(Boc)
6. Fmoc-Arg(Pmc)
7. Fmoc-Pro

to provide N-Ac-Pro-Arg-Lys-Leu-Tyr-Asp-3-I-Tyr-NH_2 (2.5 mg). MS (ESI) m/z 1121 $(M+H)^+$.

EXAMPLE 12

N-Ac-Lys-Leu-Tyr-Asp-NH_2

The title compound was prepared using the synthetic sequence described in Example 1 and using Fmoc-Asp(β-O'Bu) as amino acid No. 1. The following amino acids were added using the conditions indicated:

No. Amino Acid
2. Fmoc-Tyr('Bu)
3. Fmoc-Leu
4. Fmoc-Lys

to provide 2 mg of N-Ac-Lys-Leu-Tyr-Asp-NH_2 (2 mg).

EXAMPLE 13

Preparation and Separation of a Mixture N-Ac-Pro-Arg-Lys-Leu-Tyr-Asp-3-I^{125}-Tyr^{535}-NH_2 and N-Ac-Pro-Arg-Lys-Leu-3-I^{125}-Tyr^{533}-Asp-Tyr-NH_2 (SEQ ID NO: 6) and (SEQ NO: ID 18), Respectively

To a solution of 30 μg of N-acetyl-prolyl-arginyl-lysyl-leucyl-tyrosyl-aspartyl-tyrosylamide in 80 mL of phosphate buffered saline (PBS) was added one iodobead (Pierce, Rockford, Ill.) and 100 μCi of NaI^{125}. After 10 minutes, the excess NaI^{125} reagent was removed by applying the reaction mixture to a Waters C18-Light SepPack column and eluting with water then 0.1% TFA in 1:1 CH_3CN/water and collecting 3×200 μL fractions to provide a mixture of Tyr^{533}- and Tyr^{535}-radiolabeled peptides.

The hot peptide mixture was coinjected onto a C18 HPLC column with an equimolar solution of cold carriers N-Ac-Pro-Arg-Lys-Leu-Tyr-Asp-3-I-Tyr-NH_2 and N-Ac-Pro-Arg-Lys-Leu-3-I-Tyr-Asp-Tyr-NH_2, the elution times of which had been predetermined as 36 and 38 minutes, respectively. Repeated elutions with the solvent system in Example 1 and lyophylization of the combined, relevant fractions provided the desired compound N-Ac-Pro-Arg-Lys-Leu-Tyr-Asp-3-I-Tyr-NH_2 with a minimal impurity N-Ac-Pro-Arg-Lys-Leu-3-I-Tyr-Asp-Tyr-NH_2.

General Methodologies

EXAMPLE 14

Isolation and Purification of Kringle 5 Peptide Fragments

The kringle 5 peptide fragments were prepared from the digestion of Lys plasminogen (Lys-HPg, Abbott